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(54) **Novel synergistic agricultural insecticidal and acaricidal combinations containing avermectin derivatives**

(57) Novel combinations of agricultural insecticides, acaricides and pesticides have a synergistic effect against such agricultural insect and mite pests. Avermectin amino and alkylated amino derivates thereof, which are known to be highly effective, broad-spectrum agricultural pesticidal agents, are combined with compounds which are known to be active as agricultural insecticidal and acaricidal agents such as organotin, pyrethroid, organocarbamate, organophosphorous, insect growth regulator, formamidine and chlorinated hydrocarbon compounds. Such avermectin derivatives may also be combined with chitin synthesis inhibitors, ovicides, metabolic inhibitors, feeding stimulants and natural insecticidal agents. In combination, effects are observed which are greater than what could be expected from the individual compounds. Compositions containing such a synergistic combination of compounds as active ingredients are also disclosed.

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TITLE OF THE INVENTION

NOVEL SYNERGISTIC AGRICULTURAL INSECTICIDAL AND ARCARICIDAL COMBINATIONS

BACKGROUND OF THE INVENTION

Avermectin compounds are a series of natural products isolated from the fermentation broth of a strain of Streptomyces avermitilis. The series consists of eight compounds, four major and four minor. The compounds are disclosed in U.S. Patent 4,310,519. Certain derivatives of such compounds are also disclosed, such as the 22,23-dihydro derivatives described in U.S. Patent 4,199,569. The 13-deoxy derivatives of avermectin compounds are disclosed in U.S. Patents 4,171,314 and 4,173,571. The 4"-phosphate derivatives of the avermectin compounds with a 13-O-disaccharide group present, are disclosed in US Patent 4,469,682. In addition, the 4"-amino compounds and the 4"-alkylated amino compounds, the avermectin compounds of the instant combination, are disclosed in US patent 4,427,663.

The synergistic combinations also include organotin compounds such as Plictran (cyhexatin) and Vendex (fenbutatin oxide) disclosed in The 1981 Farm Chemicals Handbook, pages 268 and 359, respectively; synthetic pyrethroids, such as Ambush or Pounce (permethrin), Ammo or Cymbush (cypermethrin) and Pydrin or Belmark (fenvalerate), disclosed in The 1981 Farm Chemicals Handbook, pages C256, C95 and C148, respectively; chitin synthesis inhibitors such as Dimilin (diflubenzuron) disclosed in US patents; 3,748,356, 3,933,908, 3,989,842, and The 1981 Farm Chemicals Handbook, page C115, and Nomolt (teflubenzuron) disclosed in Technical Information Sheet of CME134 Celamerck, Ingelheim/Rhein, Germany; ovicides such as Savey (hexythiazox) disclosed in The 1987 Farm Chemicals Handbook, page C137, and Apollo (clofentezine) disclosed in The 1987 Farm Chemicals Handbook, page C64; metabolic inhibitors such as Butacide (piperonyl butoxide) disclosed in The 1987 Farm Chemicals Handbook, pages E20 and E78, triphenyl phosphate disclosed in US patent 2,805,240; feeding stimulants such as Coax disclosed in The 1987 Farm Chemicals Handbook, page C65; and natural insecticides such as Dipel (Bacillus thuringiensis) as disclosed in J. Agr. Food Chem 7, 687 (1959); organocarbamate compounds, such as Lannate (methomyl) disclosed in The 1981 Farm Chemicals Handbook, page C215, Larvin (thiodicarb) disclosed in The 1987 Farm Chemicals Handbook, pages C250 and E72, and Furadan (carbofuran) disclosed in The Pesticide Manual, Worthing (Ed.) (1979) page 82; organophosphorous compounds, such as Orthene (acephate), Lorsban

(chlorpyrifos), Thimet (phorate), Basudin (diazinon) and methylparathion disclosed in The 1981 Farm Chemicals Handbook, pages C246, C77, C262, C107 and C218, respectively; malathion, disclosed in The 1987 Farm Chemicals Handbook, pages C155 and E66, dimethoate disclosed in The 1987 Farm Chemicals Handbook, pages C91 and E23, and Padan (cartap) disclosed in The Pesticide Manual, Worthing (Ed.) (1979) page 86; insect growth regulators, such as Dimilin (diflubenzuron), also useful as an chitin synthesis inhibitor and discussed above; formamidine compounds, such as Mitac (amitraz) and Fundal (chlordimeform) disclosed in The 1981 Farm Chemicals Handbook, pages C17 an C70, respectively, and chlorinated hydrocarbon compounds such as Kelthane (dicofol) and Acarol (bromopropylate) disclosed in The 1981 Farm Chemicals Handbook pages C110 and C115, respectively, and Thiodan (endosulfan) disclosed in US patent 2,983,732.

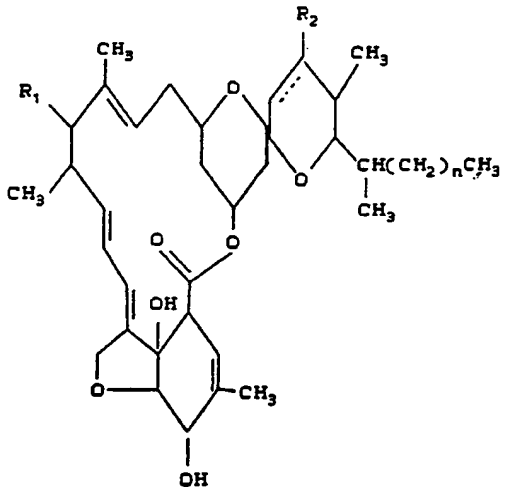
SUMMARY OF THE INVENTION

The instant disclosure describes certain synergistic combinations of avermectin compounds and organotin, pyrethroid, chitin synthesis inhibitor, ovicide, metabolic inhibitor, feeding stimulant, organocarbamate, organo-phosphorous, insect growth regulator, formamidine, tertiary amine and chlorinated hydrocarbon compounds and natural insecticidal agents which are referred to hereinafter as "combining compounds". Thus, it is an object of this invention to describe such synergistic combinations. It is a further object to describe the individual components of such synergistic

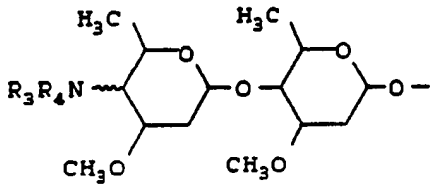
combinations and the relative proportion of each component in the combination. A still further object of this invention is to describe the agricultural, insecticidal, acaricidal and pesticidal effects of such combinations. Further objects will become apparent from a reading of the following description.

DESCRIPTION OF THE INVENTION

The instant invention consists of a combination of avermectin compounds and combining compounds which have a synergistic effect when used in the control or elimination of infestations in domestic and agricultural environments. The avermectin compounds of this invention have the following formula:



wherein n is 0 or 1;
$R_1$ is



$R_2$ is hydrogen;
the broken line indicates a single or a double bond; however, $R_2$ is present only when the broken line indicates a single bond; and
$R_3$ and $R_4$ are independently hydrogen or loweralkyl.

The preferred avermectin compound is the 4"-epimethyl amino derivative of avermectin B1a/B1b. That is the compound wherein $R_3$ is hydrogen, $R_4$ is methyl; the 4"-amino stereochemistry is ß, above the plane of the ring (the natural stereochemistry for the avermectin is α, below the plane of the ring); and n is both 0 and 1, that is the compound which is a mixture of the sec. butyl compound (n = 1) and the isopropyl compound (n = 0), in approximately an 80:20 ratio of sec-butyl to isopropyl compounds.

The combining compounds that constitute the second part of the instant synergistic combinations are exemplified by the representative compounds disclosed above in the Background of the Invention.

When used as agricultural insecticide or miticides the avermectin compounds are administered at dosage rates of from 1.0 to 50 g of the active

compound per hectare. When used as agricultural insecticide agents the combining compounds are administered at dosage rates of from 10 to 2500 g of the active compound per hectare.

The synergistic effects of the combination of the avermectin compounds with the combining compounds are observed in providing for a reduced dosage of one or both of the components. Thus, a lessened quantity of the agricultural insecticide or acaricide is administered than normally would be required which results in a lessening of possible side effects and a lessening in the development of resistance. In addition, there is observed the synergistic expansion of the spectrum of activity on agricultural insect or mite pests which may be successfully combatted than would be expected from a consideration of the spectra of activity of the individual components. Thus, the possibility of eliminating agricultural insect and mite infestations against which the individual components are ineffective or only partially effective is realized in the instant synergistic combination.

The agricultural arthropod infestations against which the instant synergistic combination is particularly effective are Acarina such as Tetranychus urticae, Panonychus ulmi, Panonychus citri, Phyllocoptruta oleivora and Polyphagotarsonemus latus; and the like; Coleoptera such as Leptinotarsa decemlineata, Phyllotrecta striolate; Lepidoptera such as Spodoptera exiqua, Plutella xylostella, Pieris rapae, Heliothis virescens and H. zea; Diptera such as Liriomyza trifolii; Homoptera such as Psylla pyricola, Myzus pescicae, Brericoryne brassicae,

Bemisia tabaci and Aphis gossypii, and the like; Orthoptera such as Blattella germanica.

The instant synergistic combination is useful for controlling the above mite pests, and others, on economically useful crops such as maize, vegetables, cotton, deciduous fruit, citrus, tree nuts and vines.

In using the instant synergistic combination, the individual components are used in proportions which may extend to from 1 part of the avermectin compound to 2500 parts of combining compound to from 100 parts of the avermectin compound to 1 part of combining compound.

The synergistic composition is useful against insect and mite pests of stored grain and agricultural plants and immature stages of mites or insects living in or on plant tissue. When the synergistic composition is used to combat agricultural pests that inflict damage upon crops while they are growing or in storage, it is applied using known techniques such as sprays, granules, dusts, emulsions, and the like, to the growing plant or the soil in which it is planted, or to the stored crops to effect protection from such agricultural pests.

Specific formulations containing avermectin compounds and combining compounds which have synergistic agricultural, insecticidal, arcaricidal, pesticidal and miticidal effects are as follows:

| Formulation 1 | Weight % |
|---|---|
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b | 2.00 |
| Dicofol | 20.00 |
| Xylenes | 60.00 |
| Emulsifier | 18.00 |
| Total | 100.00 |

| Formulation 2 | Weight % |
|---|---|
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b | 2.00 |
| Acarol | 24.00 |
| Xylenes | 56.00 |
| Emulsifier | 18.00 |
| Total | 100.00 |

| Formulation 3 | Weight % |
|---|---|
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b | 2.00 |
| Chlorbenzilate | 15.50 |
| Xylenes | 65.50 |
| Emulsifier | 17.00 |
| Total | 100.00 |

| Formulation 4 | Weight % |
|---|---|
| Chlordimeform | 24.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Xylenes | 61.8 |
| Emulsifiers | 12.0 |
| Total | 100.0 |

| Formulation 5 | Weight % |
|---|---|
| Amitraz | 20.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Xylenes | 65.8 |
| Emulsifiers | 12.0 |
| Total | 100.0 |

| Formulation 6 | Weight % |
|---|---|
| Malathion | 20.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Xylenes | 65.8 |
| Emulsifiers | 12.0 |
| Total | 100.0 |

| Formulation 7 | Weight % |
|---|---|
| Dimethoate | 20.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Xylenes | 65.8 |
| Emulsifiers | 12.0 |
| Total | 100.0 |

| Formulation 8 | Weight % |
|---|---|
| Dimilin (98%) | 25.5 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.0 |
| Attaclay | 25.0 |
| Diethylene glycol | 4.0 |
| Talc | 28.0 |
| Wetting agent | 12.0 |
| Dispersing agent | 3.0 |
| Oleic acid | 0.5 |
| Total | 100.0 |

| Formulation 9 | Weight % |
|---|---|
| Dimilin (98%) | 4.08 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 0.44 |
| Granular Montmorillonite Clay | 89.48 |
| Diethylene glycol | 6.00 |
| Total | 100.00 |

| Formulation 10 | Weight % |
|---|---|
| Diazinon (87%) | 54.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Xylenes | 29.8 |
| Emulsifier | 14.0 |
| Total | 100.0 |

| Formulation 11 | Weight % |
|---|---|
| Methyl Parathion (80%) | 25.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Xylenes | 60.8 |
| Emulsifier | 12.0 |
| Total | 100.0 |

| Formulation 12 | Weight % |
|---|---|
| Chlorpyrifos | 24.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Xylenes | 61.8 |
| Emulsifier | 12.0 |
| Total | 100.0 |

| Formulation 13 | Weight % |
|---|---|
| Diazinon (87%) | 5.75 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 0.33 |
| Montmorillonite granule | 87.92 |
| Diethylene glycol | 6.00 |
| Total | 100.00 |

| Formulation 14 | Weight % |
|---|---|
| Methomyl | 24.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Attaclay | 36.3 |
| Kaolin | 16.0 |
| Wetting agent | 12.0 |
| Dispersing agent | 3.0 |
| Oleic acid | 0.5 |
| Diethylene glycol | 6.0 |
| Total | 100.0 |

| Formulation 15 | Weight % |
|---|---|
| Carbofuran | 50.0 |
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 |
| Attaclay | 19.8 |
| Kaolin | 6.5 |
| Wetting agent | 12.0 |
| Dispersing agent | 3.0 |
| Oleic acid | 0.5 |
| Diethylene glycol | 6.0 |
| Total | 100.0 |

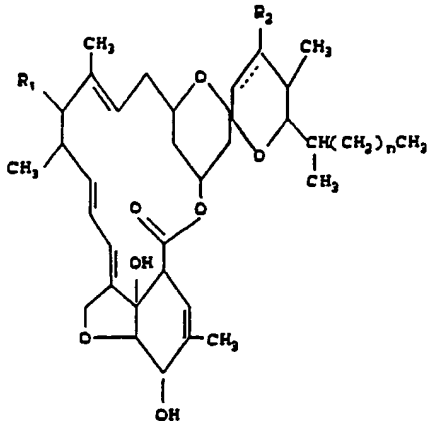
| Formulation 16 | Weight % | Weight % |
|---|---|---|
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b | 2.2 | 2.2 |
| Plictran | 50.0 | - |
| Vendex | - | 50.0 |
| Attaclay | 25.0 | 25.0 |
| Kaolin | 3.8 | 3.8 |
| Diethylene glycol | 4.0 | 4.0 |
| Wetting agent | 12.0 | 12.0 |
| Dispersing agent | 3.0 | 3.0 |
| Total | 100.0 | 100.0 |

| Formulation 17-Liquid | Weight % | Weight % | Weight % |
|---|---|---|---|
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 2.2 | 2.2 | 2.2 |
| Cypermethrin | 20.0 | - | - |
| Fenvalerate | - | 20.0 | - |
| Deltamethrin | - | - | 20.0 |
| Xylenes | 70.0 | 70.0 | 70.0 |
| Emulsifier | 8.0 | 8.0 | 8.0 |
| Total | 100.0 | 100.0 | 100.0 |

| Formulation 18-Granular | Weight % | Weight % | Weight % |
|---|---|---|---|
| 4"-epimethylamino-4"-deoxy Avermectin B1a/B1b (91%) | 0.33 | 0.33 | 0.33 |
| Avermectin B1a/B1b (91%) | 0.33 | 0.33 | 0.33 |
| Cypermethrin | 3.00 | - | - |
| Fenvalerate | - | 3.00 | - |
| Deltamethrin | - | - | 3.00 |
| Montmorillonite granule | 90.67 | 90.67 | 90.67 |
| Diethylene glycol | 6.00 | 6.00 | 6.00 |
| Total | 100.00 | 100.00 | 100.00 |

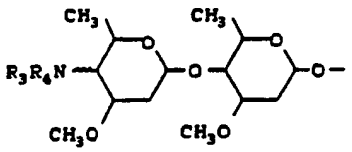
WHAT IS CLAIMED IS:

1. A synergistic agricultural, insecticidal, arcaricidal and pesticidal combination of an avermectin compound having the formula:



wherein n is 0 or 1;

$R_1$ is



$R_2$ is hydrogen;

the broken line indicates a single or a double bond; however, $R_2$ is present only when the broken line

indicates a single bond; and $R_3$ and $R_4$ are independently hydrogen or lower alkyl; and a combining compound selected from the group consisting of organotin, pyrethroid, chitin synthesis inhibitor, ovicide, metabolic inhibitor, feeding stimulant, organocarbamate, organophosphorous, insect growth regulator, formamidine, chlorinated hydrocarbon, and natural insecticidal agents.

2. The synergistic combination of Claim 1 wherein the organotin compound is cyhexatin or fenbutatin oxide; the pyrethroid compound is permethrin, cypermethrin, fenvalerate or deltamethrin; the chitin synthesis inhibitor is diflubenzuron or teflubenzuron; the ovicide is hexythiazox or clofentezine; the metabolic inhibitor is piperonyl butoxide or triphenyl phosphate; the feeding stimulant is coax; the natural insecticide is Bacillus thuringiensis; the organocarbamate compound is methomyl, dithiocarb or carbofuran; the organophosphorous compound is acephate, chlorpyrifos, phorate, diazinon, methylparathion, malathion, dimethoate; the tertiary amino is cartap; the insect growth regulator compound is diflubenzuron; the formamidine compound is amitraz or chlordimeform, and the chlorinated compound is dicofol, bromopropylate, or endosulfan wherein the compounds are present at a proportion of from 1 part of the avermectin compound to 2,500 parts of combining compound, to from 100 parts avermectin compound to 1 part of combining compound.

3. A method for the treatment of agricultural insect and mite infestations which comprises applying to an agricultural crop or commodity infected with insects or mites, the synergistic combination of Claim 1.

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